

Amendments to the Specification:

Please insert on page 1 after the title “TARGETING ENZYMES OF THE tRNA SPLICING PATHWAY FOR IDENTIFICATION OF ANTI-FUNGAL AND/OR ANTI-PROLIFERATIVE MOLECULES” the following paragraph:

This application claims benefit of United States Provisional Application No. 60/458,067, filed on March 27, 2003.

Please delete the paragraph beginning on page 102, line 16, as shown below.

~~[PLEASE PROVIDE SPECIFIC PROTOCOLS FOR PREFERRED LIGASE ASSAYS]~~

Please replace the paragraph beginning on page 102, line 18 with the following amended paragraph:

The invention encompasses methods for identifying a compound that modulates the kinase activity of an animalia or fungal tRNA splicing ligase utilizing a polynucleotide kinase assay well-known to known to one of the skill in the art. Although not intending to be bound by any mechanism of action, this assay is based on the ability of an animalia or fungal tRNA splicing ligase to transfer the γ -phosphate of ATP to a variety of polynucleotides. One exemplary assay for measuring a polynucleotide kinase activity may comprise the following: providing a poly(A) nucleotide of, for example, 600 nucleotides in length; providing [γ - ^{32}P]ATP; providing a sufficient amount of an animalia or fungal tRNA splicing ligase in an appropriate buffer including, for example, a buffer containing a DTT and MgCl_2 , which is either pre-incubated with a library of the compounds or not; allowing the reactants to incubate for 15 minutes at 37°C; phenol chloroform extracting the reaction; adding bovine serum albumin and cold trichloroacetic acid to the aqueous phase; collecting the insoluble material by centrifugation; adding cold trichloroacetic acid and sodium pyrophosphate; collecting the acid insoluble material on glass fiber filter; measuring the radioactivity on the glass filter, wherein the amount of measured radioactivity is proportional to the kinase activity of the tRNA splicing ligase. If the compound inhibits or reduces the kinase activity of the tRNA splicing ligase, the amount of radioactivity measured is decreased relative to the amount of radioactivity measured in the absence of the compound or the presence of a negative control (*e.g.*, PBS). On the other hand, if the compound increase the kinase activity of the tRNA splicing ligase, the amount of radioactivity measured is decreased relative to the amount of radioactivity measured in the absence of the compound or the presence of a negative control (*e.g.*, PBS). Polynucleotide kinases assays are well-known in

the art. *See e.g.*, Xu *et al.*, 1990, *Methods in Enzymology*, 181: 463-471; Phizicky *et al.*, 1986, *Journal of Biol. Chem.* 261(6): 2978-2986; Pick *et al.*, 1986, *J. Biol. Chem.*, 261: 6684.
~~[PLEASE CONFIRM AND PROVIDE PREFERRED KINASE ASSAY]~~